SAM-TR-69-1

A FURTHER SURVEY OF COMPOUNDS FOR RADIATION PROTECTION

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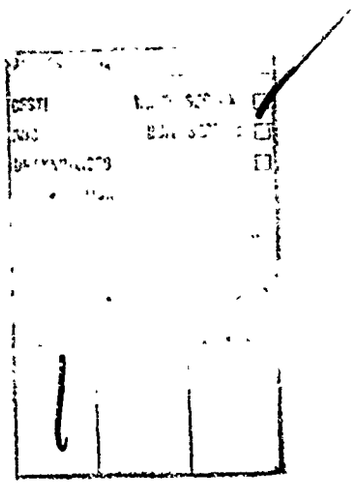
February 1969



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FOREWORD

This report was prepared at the USAF Radiation Laboratory of the University of Chicago and represents a summary of unpublished data. It is a sequel to "A Survey of Compounds for Radiation Protection" published in April 1962 as SAM-TR-62-29 by the USAF School of Aerospace Medicine. This compilation includes work accomplished from January 1961 through April 1965 under task No. 775703 and contract No. 41(609)-2977. The contract monitor was Lieutenant Colonel George S. Melville, Jr., Radiobiology Division, USAF School of Aerospace Medicine. The report was received for publication on 1 November 1968.

The animals involved in this study were maintained in accordance with the "Guide for Laboratory Animal Facilities and Care" as published by the National Academy of Sciences–National Research Council.

This report has been reviewed and is approved.

GEORGE E. SCHAFER
Colonel, USAF, MC
Commander

ABSTRACT

This report summarizes the results obtained with 617 compounds tested for their radioprotective activity in adult male mice irradiated with a control-demonstrated LD_{99+} of 800 R (250 kvp) x-rays. A compound was considered to exhibit radioprotective activity if it (1) permitted any of the treated mice to survive for 30 days after the otherwise lethal whole-body x-irradiation or (2) increased the median survival time of treated animals by 5 days or more beyond the median survival time of the untreated control mice (9 ± 3 days).

Of the 617 compounds tested, 245 successfully passed one or both of the stated specifications. Additionally, data are offered to allow comparisons of chemically related groups for structure-activity relationships, and to indicate the types of structures which offer the greatest promise as a source of more effective and less toxic radioprotective agents.

CONTENTS

A FURTHER SURVEY OF COMPOUNDS FOR RADIATION PROTECTION

I. INTRODUCTION

The purpose of the radiation screening program of the University of Chicago was to find chemical or biologic agents which exhibited prophylactic or therapeutic effectiveness against radiation injury. Testing the ability of such agents to prolong survival or to reduce lethality in x-irradiated mice was one phase of our efforts to find practical methods to modify radiation injury in animals. Other phases of the program included: (1) the investigation of the physiologic and biochemical mechanisms responsible for the toxic and protective effects of radioprotective agents in mice and other species; (2) the evaluation of the efficacy of such agents against chronic radiation exposure and against exposure to other types of ionizing radiation; and (3) the ability of various environmental and pharmacologic factors to modify either the toxic or the protective properties of single agents or of combinations of radioprotective agents.

A previous survey of approximately 1,200 compounds was published in April 1962. The present report summarizes the results that were obtained with approximately 600 compounds tested from January 1961 through April 1965. It has a twofold purpose: (1) to facilitate the comparison of chemically related groups for structure activity relationships, and (2) to indicate the types of structures which offer the greatest promise as a source of more effective and less toxic radioprotective agents. Initially, the compounds used in the testing program were selected with the idea of obtaining examples of as many different chemical types as possible. Since more information has been accumulated on potentially radioprotective agents of a rather large number of chemical types, it is now possible to depend less on the survey approach of selection and more on trying to obtain compounds designed to provide more specific data on the structure-activity relationships within each chemical type.

II. EXPERIMENTAL METHODS

Adult male mice (6 to 8 weeks old) from Carworth Farms (CF_1) were used in the studies. The average weight was from 20 to 25 gm. The mice were housed in an air-conditioned room (75° to 80° F.) and were provided with Rockland mouse pellets and water ad libitum. Both control and treated animals were selected at random from a single shipment so that their age and physical condition would be comparable. All the mice were kept under observation for at least one week before they were used. Those that appeared to be unhealthy or failed to gain weight at a normal rate were removed for autopsy.

To evaluate the radioprotective activity of the compounds, the mice were divided into groups of 10 and injected intraperitoneally 10 to 15 minutes prior to the administration of a lethal (800 R) dose of whole-body x-irradiation. Each compound was tested for protective effects at two or more dosage levels, one of which was close to the maximum tolerated dosage level for that particular compound. Distilled water was used as the vehicle whenever possible and the concentration of the solution was adjusted so that no animal received more than 2% of its body weight with each injection.

When necessary, the pH was adjusted to approximately 7.0 with either 1N HCl or 1N NaOH. Compounds which were insoluble in water or in propylene glycol (PG) were dissolved in cottonseed oil or suspended in a 0.5% solution of carboxymethylcellulose. Control animals were injected with a comparable amount of the vehicle used to prepare the solution and were irradiated simultaneously with the treated groups. The loss of weight and the mortality in both groups were recorded daily for 30 days after the x-ray exposure or until all of the mice were dead.

The radiation exposures were given as single whole-body 250 kvp, 15 ma. x-ray exposures using either a G.E. Maximar or a Keleket x-ray therapy unit. The added filtration consisted of 0.25 mm. of copper and 1.0 mm. of aluminum, and the target-skin distance was 75 cm. The dose rate in air was determined prior to each radiation period, by use of Victoreen ionization thimbles (100 R); it was found to average between 40 and 43 R per minute. The mice were placed in individual plastic tubes (50-ml. centrifuge tubes provided with numerous air holes) which, in turn, were positioned radially on a rotating turntable to equalize the dose of x-ray. The environmental temperature was maintained at 75° F. during the irradiation period to minimize the effect of variations in the environmental stress in both the control and treated groups.

III. RESULTS

Preliminary toxicity tests were conducted for each compound before the radiation studies to ascertain the maximum tolerated dose which could be given the animals without causing drug lethality. For these studies, small groups of mice were injected intraperitoneally with increasing dosage levels of each compound and the mortality observed for a week. The approximate LD_{50} (7 days) thus obtained was used as a basis for selecting the dosage levels to be used for the radiation studies.

Doses exceeding 1,000 mg. kg. were not used, since the limited size of the sample and the disadvantages of injecting an increased amount of vehicle made the larger doses impractical. The approximate LD_{50} in milligrams per kilogram for each of the compounds tested is included in the tables which comprise the remaining part of this report.

The x-ray dosage level employed (800 R) uniformly caused a mortality greater than 99% within two weeks after the exposure under our experimental conditions. Radiation deaths usually began on the fifth or sixth day after the x-ray exposure and the median survival time (ST_{50}) of untreated animals was 9 ± 3 days. A compound was considered to exhibit radioprotective activity if it increased the median survival time by 5 days or more, or if it permitted any of the treated animals to survive for 30 days after the otherwise lethal whole-body x-irradiation.

Since all of these studies were carried out by use of a single dose of x-irradiation (800 R), the results do not provide a precise quantitation of the radioprotective effect of each compound tested. However, the protective effect or dose reduction factor (DRF) resulting from the preirradiation administration of a compound can be estimated on the basis of the x-ray dosage level which would be required to produce a comparable mortality at 30 days after the irradiation exposure. The LD_{50} (30-day) value for the adult CF_1 male mice used in these studies was 542 ± 18 R. The estimated DRF values are given in table I.

TABLE I

Estimated dose reduction factors based on 30-day mortality data

Percent survival*	DRF†
10 to 20	1.3
30 to 40	1.4
50 to 60	1.5
70 to 80	1.6
90 to 100	1.7

*Percent of treated animals surviving at 30 days after 800 R x-irradiation.

†Administered radiation dose divided by effective radiation dose.

In the tables which comprise the remaining part of the report the compounds are listed in order of increasing complexity within each of the chemical types. The name of each compound is listed with the vehicle used.[1] In the radiation studies the change in ST_{50} indicates the increase or decrease (in days) of the median survival time of the treated animals when compared to that of the simultaneously irradiated control (vehicle only) groups.

[1]The symbol representing vehicle (e.g., HOH) appears in parentheses below the name of the compound.

ALCOHOLS AND THIOLS

Compound and vehicle used for toxicity and radiation tests	Toxicity	Radiation studies		
	Approx. LD_{50} (mg./kg.)	Dose (mg./kg.)	Change in ST_{50} (days)	Mortality at 30 days
2-Methylaminoethanol (HOH)	250	200	−4	10/10
		100	0	10/10
1-Amino-2-propanol (HOH)	400	300	−10	10/10
		100	−4	10/10
Acetone sodium bisulfite (HOH)	> 1000	1000	+2	10/10
		500	--3	10/10
Glyoxal (30% in water) (HOH)	750	500	−5	9/10
		300	+3	5/10
Propylene glycol (1,2-propanediol) (100%)	17500	3000	+2	10/10
		5000	0	8/10
		6250	+2	9/10
		7500	−3	10/10
		8750	−4	10/10
		10000	−3	10/10
		12500	−7	10/10
2-Isobutylaminoethanol (HOH)	250	200	−3	10/10
		100	−2	10/10
2,3-Butanediol (HOH)	> 1000	1000	−1	10/10
		500	−2	10/10
Batyl alcohol (PG)	750	500	−1	10/10
		250	−2	10/10
3-(N-Methylisopropylamino)-3-methyl-2-butanol hydrochloride (HOH)	250	200	0	10/10
		100	−5	10/10
		50	−8	10/10
Calcium gluconate (HOH)		10	0	10/10
2-Amino-1-phenyl-1-ethanol (HOH)	250	200	−5	10/10
		100	−9	10/10
2,6-Dimethylphenol (PG)	150	100	0	10/10
		50	−1	10/10
2,4-Di-tert-butylphenol (PG)	25	10	−3	10/10
		5	−2	10/10
N-Propyl-p-hydroxybenzoate (PG)	200	100	−1	10/10
		50	0	10/10

Sodium-p-hydroxyphenylarsonate (HOH)	1000	500 200	−6 +2	10/10 10/10
p-Methoxyphenol (PG)	250	200 100	−4 0	9/10 10/10
2-Methoxy-4-n-pr pyrphenol (PG)	150	100 50	−9 +2	10/10 7/10
m-Chloroacetylcatechol (HOH)	75	50 25	−6 +6	10/10 10/10
Pyrogallol (HOH)	400	300 100	−3 +2	10/10 10/10
Desoxypyridoxine hydrochloride (HOH)	150	100 50	−5 0	10/10 10/10
o-Aminophenol (PG)	200	100 50	−1 0	10/10 10/10
m-Aminophenol (PG)	150	100 50	0 −1	10/10 10/10
p-Nitrophenol (PG)	75	50 25 10	−2 −2 −2	10/10 10/10 10/10
p-Aminophenol hydrochloride (HOH)	750	500 300	−2 −4	10/10 10/10
4-Amino-3-methylphenol (PG)	200	100 50	−1 −2	10/10 10/10
p-Phenylphenol (PG)	150	100 50	−2 0	10/10 10/10
p-Hydroxydiphenyl (PG)	150	100 50	0 0	10/10 10/10
Naphthoresorcinol (PG)	200	100 50	0 0	8/10 10/10
o,o'-Biphenol (PG)	150	100 50	−1 −3	10/10 10/10
2,2'-Dipropyl-p,p'-biphenol (PG)	40	25 10	0 +1	10/10 10/10
4,4'-Di-tert-butyl-o,o'-biphenol (PG)	50	40 25	−6 −5	10/10 10/10
2,2'-Diallyl-p,p'-biphenol (PG)	100	50 25	−4 −2	10/10 9/10
p,p'-Isopropylidene-diphenol (PG)	150	100 50	−10 −9	10/10 10/10

4,4'-Isopropylidene-bis(2-tert-butylphenol) (PG)	40	25 10	−5 −6	10/10 10/10
p,p'-Oxydiphenol (PG)	150	100 50	−5 −4	10/10 10/10
p-Phenylazophenol (PG)	75	50 25	−3 −3	10/10 10/10
3-Methyl-4-phenylazophenol (PG)	25	10 5	+1 −1	10/10 10/10
Hydroquinone (HOH)	150	100 50	+3 0	8/10 10/10
2-Quinolinol (PG)	150	100 50	>+18 >+22	3/10 4/10
8-Quinolinol (PG)	50	25 10	+9 +1	5/10 9/10
2',5'-Salicyloxylidide, 3-nitro (PG)	25	10 5	+1 −1	10/10 10/10
2',6'-Salicyloxylidide, 3-nitro (PG)	40	25 10	−2 +6	10/10 7/10
o-Salicylotoluidide, 3,5'-dinitro (PG)	100	100 50	+5 +3	10/10 9/10
α-Benzoinoxime (PG)	150	100 50	−5 0	10/10 10/10
α-Thioglycerol (HOH)	400	300 100	0 +1	10/10 10/10
Thioglycolic acid – 98% (HOH)	150	100 50	−5 −1	10/10 10/10
Thiodiglycolic acid – 98% (HOH)	250	200 100	−6 0	10/10 10/10
Thiomalic acid (HOH)	500	300 100	−4 +1	10/10 10/10
Methylmercaptoacetate (HOH)	400	100 50	+5 −2	10/10 10/10
1,2-Bis-(β-mercaptoethylaminomethyl) cyclobutane (HOH)	250	200 100	>+18 +1	4/10 7/10
6-Methylthio-m-cresol (PG)	125	100 50	>+19 +1	3/10 9/10
4-Methylthio-m-cresol (PG)	150	100 50	>+19 −1	3/10 8/10

p-Chlorobenzenethiol (PG)	75	50 25	−4 +1	10/10 10/10
p-Dimethylaminobenzenethiol (PG)	150	100 50	−3 −2	8/10 9/10
1-Mercaptoanthraquinone (PG)	750	500 300	> +21 +2	4/10 10/10
1-Hydroxy-4-thiophenylanthraquinone (HOH and PG)	500	100 50	−2 +2	10/10 10/10
1-Amino-2-thiophenyl-4-hydroxyanthra-quinone (PG and sesame oil)	200 750	500 300	−2 +1	10/10 10/10
Phenylmercaptodiaminoanthrarufin (PG and sesame oil)	150 300	300 200	−1 +1	10/10 10/10
1-Amino-2-tert-butylphenylmercapto-4-hydroxyanthraquinone (PG)	250	200 100	+1 +1	10/10 10/10
Thioflavine S (HOH)	400	300 100	−2 +1	10/10 10/10

ETHERS

Compound and vehicle used for toxicity and radiation tests	Toxicity	Radiation studies		
	Approx. LD_{50} (mg./kg.)	Dose (mg./kg.)	Change in ST_{50} (days)	Mortality at 30 days
1-Methoxy-2-amino-2-methylpropane (HOH)	400	300 100	−7 0	10/10 10/10
Bis(2-nitroisobutyl)-2-ethylhexyl phosphate (HOH)	250	200 100	−1 +3	10/10 10/10
N-(3-Butoxypropyl)taurine, monosodium salt (HOH)	1000	1000 500	+4 +2	7/10 8/9
Cyclobutane-1,2-bis(methylammonium phosphate (HOH)	1000	1000 500	−3 +2	10/10 10/10
Cyclobutane-1,2-bis(methylammonium) dimonochloroacetate (HOH)	200	100 50 25	−4 −2 +3	10/10 10/10 9/10
β-Hydroxyethylbenzyl ether (PG)	250	200 100	0 +1	7/10 10/10
β-Hydroxyethyl ether of orthocresol (PG)	250	200 100	−3 +1	9/10 9/10
β-Hydroxyethyl ether of butylphenol (PG)	100	50 25	−1 −3	9/10 10/10
β-Hydroxyethyl ether of m-xylenol (PG)	150	100 50	−5 −1	10/10 10/10
p-Dimethoxybenzene (PG)	400	300 100	−7 +1	10/10 8/10
p-Nonylphenyl-β-dimethylaminoethyl ether (PG)	150	100 50	−6 −1	10/10 9/10
1,6-Bis(p-aminoethylphenoxy)hexane dihydrochloride (HOH)	100	50 25	−4 −3	10/10 7/10
1,6-Bis(p-methylaminomethylphenoxy) hexane dihydrochloride (HOH)	150	100 50	−2 0	9/10 8/10
Phenylmercurilauryl thioether (PG)	500	300 200	−3 0	9/10 9/10
2-Methyl-2-nitro-1-propyltosylate (PG)	250	200 100	+1 +3	10/10 10/10

Bis-[p-(α-diethylaminopropoxy)phenyl] sulfone (HOH)	75	50 25	−1 +1	10/10 10/10
Bis-p-phenyl methane sulfone (PG)	200	100 50	+1 −3	6/10 10/10
β-Naphthylethyl ether (PG)	100	50 25	−2 0	10/10 10/10
β-Hydroxyethyl ether of β-naphthol (PG)	150	100 50	−5 −1	9/10 7/10
β-Hydroxyethyl ether of orthophenylphenol (PG)	75	50 25	+2 +1	7/10 8/10

KETONES AND PHENONES

Compound and vehicle used for toxicity and radiation tests	Toxicity	Radiation studies		
	Approx. LD_{50} (mg./kg.)	Dose (mg./kg.)	Change in ST_{50} (days)	Mortality at 30 days
Methylallyl acetone (HOH)	1000	500 300	+1 −4	10/10 10/10
Acetylacetone (HOH)	750	500 300	−2 −6	10/10 10/10
p-Benzoquinone (HOH)	7.5	5 1	−2 −2	10/10 10/10
2-Methylcyclohexanone (PG)	200	100 50	+1 −5	10/10 10/10
Pulegone (PG)	150	100 50	−1 +2	10/10 7/10
Acetone oxime (PG)	250	200 100	0 +2	10/10 10/10
2-Butanone oxime (PG)	1000	1000 500 250	−4 >+18 +2	10/10 3/10 10/10
Di(methylcyclopropyl)ketoxime (HOH)	250	200 100	−2 0	10/10 9/10
Cyclohexanone oxime (PG)	250	200 100	−2 0	10/10 10/10
Isonitrosopropiophenone (Lot No. FI-9) (PG)	250	200 100	0 −2	10/10 10/10
6-Amino-5-hydroxyimino-1,3-dimethyl hydrouracil (PG)	250	200 100	+1 −1	10/10 10/10
Pyridine-2-aldoxime (PG)	200	100 50	+3 +1	10/10 8/10
Pyridine-3-aldoxime (HOH)	200	100 50	+3 −1	10/10 10/10
Pyridine-4-aldoxime (PG)	150	100 50	+4 +6	10/10 9/10
Isonitrosopropiophenone (Lot No. EL-152) (PG)	200	100 50	+1 +8	7/10 8/10
Pyridine-2-aldoxime o-benzyl ether (PG)	100	50 25	+3 +3	10/10 10/10

2,3,4a,5,8,8a-Hexahydro-1,4-naphthoquinone (PG)	200	100 50	>+22 0	4/10 10/10
Methylnaphthoquinone (PG)	15	10 5	+4 +2	7/10 10/10
2-Methyl-1,4-naphthoquinone (Menadione) (PG)	50	40 25	−5 −2	10/10 10/10
7-Chloro-4-(3-octylaminopropyl)amino-quinoline,1-oxide (PG)	40	25 10	−2 +2	10/10 10/10
Sodium β-naphthoquinone-4-sulfonate (HOH)	625	300 200	−4 0	10/10 10/10
2-Oxo-3-isobutyl-9,10-dimethoxy-1,3,4,6,7,11-β-hexahydro-2H-benzoquinolizine (PG)	250	200 100	+3 +5	10/10 10/10
N-1-Anthraquinonyl-2,3-dichloropropion-amide (PG)	200	100 50	−2 +1	10/10 10/10
1-Thiophenylanthraquinone (Sesame oil)	500	500 300	−1 +2	10/10 10/10
2-Thiophenylanthraquinone (PG)	150	100 50	−3 +3	10/10 10/10
1-Amino-2-thiophenylanthraquinone (PG)	>1000	500 300	+2 +4	10/10 10/10
1-Amino-4-thiophenylanthraquinone (PG)	>1000	500 300	0 +3	10/10 10/10
Dimethylsulfoxide (DMSO) (100%)	7500	5000 2500	>+22 +4	1/10 8/10
Tetramethyldiaminothiobenzophenone (PG)	250	200 100	+3 −1	10/10 10/10
2-Nitro-4-acetyl-2'-aminodiphenyl sulfide (PG)	150	100 50	+4 −5	10/10 10/10
1-Amino-2-benzylmercapto-4-hydroxy-anthraquinone (PG)	150	100 50	−1 +4	10/10 10/10

ACIDS AND THIOACIDS

Compound and vehicle used for toxicity and radiation tests	Toxicity	Radiation studies		
	Approx. LD_{50} (mg./kg.)	Dose (mg./kg.)	Change in ST_{50} (days)	Mortality at 30 days
Cacodylic acid (HOH)	750	500 200	−3 +4	10/10 6/10
Cyanoacetic acid (HOH)	200	100 50	−5 −3	10/10 10/10
Ethylenediaminetetraacetic acid (EDTA) (PG)	250	200 100	−1 +2	10/10 10/10
Bis(diaminoethyl ether)-N,N,N′-N′-tetraacetic acid (PG)	250	200 100	−4 +1	10/10 9/10
Ethyleneglycol-bis-(aminoethyl ether) tetraacetic acid (PG)	150	300 200	−10 −1	10/10 10/10
Levulinic acid (HOH)	450	300 100	−10 >+22	10/10 4/9
Chrysanthemummonocarboxylic acid (PG)	150	100 50	−5 −1	10/10 10/10
3-Methylenecyclobutanecarboxylic acid (HOH + $NaHCO_3$)	750	500 300 100	−4 0 −1	10/10 10/10 10/10
2-Aminocyclobutanecarboxylic acid hydrochloride (HOH)	>1000	1000 500 200	−4 −3 0	10/10 10/10 10/10
trans-1,2-Cyclobutanedicarboxylic acid (HOH)	400	300 200	0 −1	9/10 10/10
3-Methyl-2-cyclobutene-1,2-dicarboxylic acid (HOH)	200	100 50	0 0	9/10 10/10
1,2-Diaminocyclohexanetetraacetic acid (PG)	150	100 50	−3 −2	10/10 9/10
Trisodium-2-(hydroxycyclohexyl)ethylenediamine triacetate (PG)	400	300 200	−4 +3	10/10 9/10
α-Imino-p-methoxybenzylmercaptoacetic acid (PG)	250	200 100	−7 0	9/10 10/10

Indole-3-acetic acid (PG)	150	100 50	+1 +3	10/10 10/10
N-(2,3-Xylyl)anthranilic acid: mefenamic acid (PG)	200	100 50	+1 −2	10/10 10/10
N-(3,5-Dichloro-p-tolyl)anthranilic acid (HOH + $NaHCO_3$)	100	50 25	0 −1	7/10 8/10
N-(α,α,α-Trifluoro-m-tolyl)anthranilic acid; flufenamic acid (PG)	150	50 25	+3 +1	10/10 10/10
N-(3-Sulfamoyl-2,6-xylyl)anthranilic acid (HOH + $NaHCO_3$)	400	300 200	+3 +2	7/8 10/10
Ethylenediamine-di(o-hydroxyphenyl)acetic acid (PG)	350	100 50	−1 −1	10/10 10/10
N-(8-Amino-1-anthraquinonyl)anthranilic acid (HOH + $NaHCO_3$)	750	500 300	−5 −8	9/10 8/10
3-(2-Aminoethylthio)propionic acid (HOH)	>1000	500 300	−5 −5	10/10 10/10
meso-2,3-Dimercaptosuccinic acid (HOH)	500	300 200	−7 −1	10/10 10/10
5,8,11,14-Eicosatetranoic acid (PG)	75	50 25	−5 −1	10/10 10/10
2-Brom-D-lysergic acid diethylamide (HOH)	75	25 10	−2 0	10/10 10/10
2-Aminoethanethiosulfuric acid (HOH)	400	300 100	+3 +3	7/10 9/10
3-Chloro-1-propanesulfonic acid, monosodium salt (HOH)	750	500 200	+6 +2	6/10 9/10
2-Carboxyphenylthioglycolic acid (HOH)	250	200 100	−8 −3	9/10 9/10
4-Chloro-2-methylphenylthioglycolic acid (PG)	150	100 50	−11 −2	10/10 10/10
Alanine: 2-methyl- (HOH)	750	500 300	−1 −1	10/10 10/10
DL-β-(3,4-Dihydroxyphenyl)alanine (HOH)	500	300 200	−1 0	10/10 10/10

L-Cysteine hydrochloride (HOH)	1250	1000 500	−6 −5	10/10 10/10
N-Acetyl-n-cysteine (HOH)	400	300 200	−4 0	10/10 10/10
(Carboxymethyl)trimethylammonium-N-acetyl-L-cysteinate (HOH)	>1000	1000 500	0 0	10/10 10/10
Glutathione (HOH)		1000	+1	10/10
Glutathione ascorbate, 63.57%-36.43% (HOH)	>100	100 50	+2 +1	9/10 9/10
Glutathione ascorbate, 1:10 (HOH)	>100	100 50	+2 −1	10/10 10/10
Glutathione ascorbate with calcium phytate (CaMg inositol hexaphosphate) (HOH)	>100	100 50	+2 −2	10/10 10/10
Glutathione (glutamyl-cysteinyl-glycine, in molecular relation) (HOH)	>100	100 50	+2 0	9/10 10/10
N-Acetyl-DL-penicillamine (PG)	400	300 200	−4 +1	10/10 10/10

ESTERS

Compound and vehicle used for toxicity and radiation tests	Toxicity	Radiation studies		
	Approx. LD_{50} (mg./kg.)	Dose (mg./kg.)	Change in ST_{50} (days)	Mortality at 30 days
Methyl chloroformate (HOH)	40	25 10	0 −5	10/10 10/10
Acetic acid: 2-methoxy-1-methyl ethyl ester (HOH)	750	500 200	+1 −5	10/10 10/10
3-(Amidinothio)propionic acid, ethyl ester, monohydrochloride (HOH)	250	200 100	+2 −2	10/10 10/10
Nitriloacetic acid trisodium salt monohydrate (HOH)	500	300 100	−3 +2	10/10 10/10
Dipotassium methanearsonate (HOH)	750	500 200	−4 +1	10/10 10/10
Monoammonium methanearsonate (HOH)	>1000	1000 500	−3 −3	10/10 10/10
Sodium cacodylate (HOH)	>1000	1000 500	−5 −4	10/10 10/10
Calcium methanearsonate (HOH)	500	300 100	−3 +1	10/10 10/10
Magnesium cacodylate (HOH)	750	500 200	−4 −3	10/10 10/10
Magnesium methanearsonate (HOH)	>1000	1000 500	0 −1	10/10 10/10
Dimercurous methanearsonate (HOH)	75	50 10	−11 −7	10/10 10/10
Disodium methanearsonate (HOH)	>1000	1000 500	−5 −2	10/10 8/10
Copper methanearsonate (HOH + $NaHCO_3$)	15	10 5	−6 +2	10/10 9/10
Dibutyl fumarate (PG)	250	200 100	+1 +2	10/10 10/10
Di-2-ethylhexyl fumarate (PG)	250	200 100	+1 +1	10/10 10/10
Dibutyl maleate (PG)	150	100 50	−1 +2	10/10 10/10

Di-2-ethylhexyl maleate (PG)	>1000	1000 500	+1 0	10/10 10/10
Ethyl-1-methyl propyl diethyl malonate (PG)	200	100 50	+1 −2	10/10 10 10
Dimethyl-1,2-cyclobutanedicarboxylate (HOH)	>1000	1500 1000 500	+2 −2 0	9/10 8 10 10/10
cis-1,2-Diisopropylcyclobutanedicarboxylate (PG)	750	500 300 100	−4 −4 +5	10 10 10/10 5/10
trans-1,2-Diisopropylcyclobutanedicarboxylate (PG)	250	200 100	−3 +2	10/10 10/10
Diisodecyl-1,2-cyclobutanedicarboxylate (PG)	750	500 300	0 0	10/10 9 10
Hexamethylenediammonium cyclobutane-1,2-dicarboxylate (HOH)	>1000	1000 500	0 +2	10/10 10/10
Cyclobutane-1,2-bis(methylammonium) adipate (HOH)	>1000	1000 500	−3 −1	10 10 10/10
Bis-(2,4,5-trichlorophenyl)-1,2-cyclobutane dicarboxylate (PG)	250	200 100	0 +2	10 10 10/10
Methyl-p-nitrobenzoate (PG)	200	100 50	0 −2	9/10 10/10
Ethyl-p-nitrobenzoate (PG)	250	200 100	0 +2	10 10 10/10
Ethyl-N-(p-nitrobenzenesulfonyl)urethane (PG)	200	100 50	−3 +16	9 10 5/10
Ethyl-N-o-toluenesulfonylurethane (PG)	250	200 100	+6 +1	8/10 10/10

AMIDES AND THIOAMIDES

Compound and vehicle used for toxicity and radiation tests	Toxicity	Radiation studies		
	Approx. LD_{50} (mg./kg.)	Dose (mg./kg.)	Change in ST_{50} (days)	Mortality at 30 days
N,N-Dimethylacetamide (HOH)	>1000	1000 500	+1 0	10/10 10/10
Acetamide: 2-(2-hydroxyethoxy)- (PG)	100	50 25	+2 −6	10/10 10/10
α-Cyanoacetamide (HOH)	>1000	1000 500	−3 0	10/10 10/10
α-Methylmercapto-α,α-diethylacetamide (PG)	750	500 200	−5 +2	10/10 10/10
α-Ethylmercaptoisobutyramide (PG)	>1000	1000 500	+5 −3	6/10 10/10
α-Allylmercaptoisobutyramide (PG)	250	200 100	0 +1	10/10 10/10
α-Allylmercapto-α,α-diethylacetamide (PG)	400	250 100	−2 0	10/10 10/10
α-Isopropylmercaptoisobutyramide (PG)	750	500 200	−1 +3	10/10 10/10
N-Acryloyltaurine, monosodium salt (HOH)	>1000	1000 500	0 +2	10/10 10/10
N-Methyl-α-crotylmercaptoisobutyramide (PG)	750	500 300	−7 −1	10/10 10/10
α-Propargylmercapto-α,α-diethylacetamide (PG)	250	200 100	−1 −3	9/10 10/10
α-Butylmercaptoisobutyramide (PG)	250	200 100	−1 −1	10/10 10/10
2,2'-Thio-bis-acetamide (PG)	625	500 300	+2 +3	10/10 10/10
trans-1,2-Cyclobutanedicarboxamide (HOH)	>1000	1000 500	+1 +1	10/10 10/10
N,N'-di-tert-Butylcyclobutane-1,2-dicarboxamide (PG)	250	200 100	−2 +2	10/10 10/10
N,N'-Bis(1,1,3,3-tetramethylbutyl)-1,2-cyclobutanedicarboxamide (PG)	250	200 100	0 −4	10/10 10/10

N,N'-(α-Naphthyl)-1,2-cyclobutanedicarboxamide (PG)	275	250 200 100	−6 +2 - 4	10/10 6/10 10/10
N,N'-(β-Naphthyl)-1,2-cyclobutanedicarboxamide (PG)	>1000	500 300	+2 −5	6/10 10/10
o-Hydroxy-N,N-diethylbenzamide (PG)	200	100 50	−2 −3	10/10 10/10
p-Toluenesulfanamide (PG)	250	200 100	−2 +3	10/10 10/10
Carbutamide (PG)	250	200 100	−1 +3	10/10 8/10
4',3-Dinitrosalicylanilide (PG)	25	10 5	−2 +3	10/10 10/10
4'-Chloro-3-nitrosalicylanilide (PG)	15	10 5	0 +2	9/10 10/10
4'-Chloro-5-nitrosalicylanilide (PG)	40	25 10	0 +4	10/10 9/10
3'-Chloro-3-nitrosalicylanilide (PG)	8	5 1	+3 0	8/10 10/10
3'-Chloro-5-nitrosalicylanilide (PG)	15	10 5	+1 +3	9/10 10/10
4'-Fluoro-3-nitrosalicylanilide (PG)	15	10 5	−7 +6	10/10 10/10
4'-Bromo-3-nitrosalicylanilide (PG)	15	10 5	0 +5	10/10 10/10
3'-Iodo-3-nitrosalicylanilide (PG)	15	10 5	+3 0	10/10 10/10
4'-Iodo-3-nitrosalicylanilide (PG)	15	10 5	−3 +4	10/10 10/10
3',4'-Dichloro-3-nitrosalicylanilide (PG)	15	10 5	+3 +8	10/10 8/10
2'-Chloro-5'-trifluoromethyl-3-nitrosalicylanilide (PG)	8	5 1	0 +2	10/10 10/10
N-p-Toluenesulfonyl, isoquinuclidylformamide (PG)	150	100 50	−4 −7	8/10 10/10

N,N-Bis(2-cyanoethyl)-N-4-hydroxy-1-anthraquinonylsulfonilamide (PG)	400	300 100	+2 −3	8/10 10/10
Bis-(2-amino-4-sulfonamidophenyl) disulfide (PG)	150	100 50	−4 −1	10/10 10/10
N,N'-Bis(2-methoxyethyl)dithiooxamide (PG)	400	250 100	0 +3	10/10 9/10
N,N'-Di-tert-butyldithiooxamide (PG)	40	25 10	−2 +2	10/10 10/10
N,N'-Dioctadecyldithiooxamide (PG)	150	100 50	0 +7	10/10 6/10
Bis-didodecyldithiooxamide (PG)	250	200 100	−4 0	10/10 10/10
Thiopyrazinamide (PG)	150	100 50	0 −2	10/10 10/10
p-Aminothiobenzamide (PG)	75	50 25	0 −3	10/10 10/10
N,N-Dimethyl-α,α-diphenylthioacetamide (PG)	250	200 100	−5 −1	10/10 10/10
N,N'-Methylene-bis-(thioisonicotinamide; hydrate (PG)	250	200 100	−6 −1	10/10 10/10

CARBAMATES AND THIOCARBAMATES

Compound and vehicle used for toxicity and radiation tests	Toxicity	Radiation studies		
	Approx. LD_{50} (mg./kg.)	Dose (mg./kg.)	Change in ST_{50} (days)	Mortality at 30 days
Dimethylcarbamyl chloride (HOH)	>1000	1000 500	−2 +2	10/10 10/10
Diethylcarbamyl chloride (HOH)	750	500 300	−1 +1	10/10 10/10
Ethyl-N,N-di-N-butylcarbamate (PG)	150	100 50	−8 −7	10/10 10/10
Ethyl-N,N-butylcarbamate (PG)	250	200 100	−4 0	10/10 8/10
Carbamic acid: 2-aminoethyl ester (HOH)	>1000	1000 500	+3 −1	10/10 10/10
N,N'-Dicarbamylformamidine (PG)	250	200 100	+1 −2	8/10 10/10
2-Nitro-2-methyl-1,3-propanedioldicarbamate (HOH)	>1000	1000 500	−3 −3	10/10 10/10
1,2-Cyclobutanedimethylcarbamate (PG)	>1000	1000 500	0 +3	9/10 10/10
1-Methylammonium-2-carbamylmethyl cyclobutane (HOH)	750	500 300	−3 +2	9/10 10/10
γ-Phenylpropylcarbamate (PG)	150	100 50	−4 0	10/10 10/10
Isopropyl-N-phenylethylcarbamate (PG)	150	100 50	−4 −4	10/10 10/10
Ethyl-N-(m-nitrophenylsulfonyl)carbamate (PG)	100	50 25	−10 −4	10/10 10/10
Ethyl-N-(p-chlorophenyl)carbamate (PG)	150	100 25	−6 0	10/10 6/10
2-Nitroisobutyl-N-phenylcarbamate (PG)	750	500 200	−2 −5	10/10 10/10
2-Nitro-2-methyl-1,3-propanediol-bis(N-phenylcarbamate) (PG)	150	100 50	−2 −3	9/10 10/10

n-Amyl-N-butylsulfonylcarbamate (sodium salt) (HOH)	750	500 200	−5 −1	10/10 10/10
Ethyl-N-(n-octylsulfonyl)carbamate (PG)	150	100 50	+6 −2	7/10 10/10
1-Methylammonium-2-dithiocarbamyl methylcyclobutane (HOH)	1000	300 100	+1 0	10/10 10/10
Thiocarbamic acid, p-hydroxyphenyl ester (PG)	150	100 50	+3 −1	7/10 10/10

Compound and vehicle used for toxicity and radiation tests	Toxicity	Radiation studies		
	Approx. LD_{50} (mg./kg.)	Dose (mg./kg.)	Change in ST_{50} (days)	Mortality at 30 days
Acetylurea (HOH)	>1000	1000 500	0 0	10/10 10/10
2-Allyl-2-thiopseudourea, monohydrobromide (HOH)	250	200 100	−1 +2	10/10 10/10
2-Methyl-2-thiopseudourea, monohydrobromide (HOH)	750	500 300	>+17 >+19	3/10 2/10
2-Methyl-2-thiopseudourea sulfate (HOH)	400	300 300 100	>+22 >+22 +7	3/10 1/9 6/10
2,2'-Trimethylene-bis(2-thiopseudourea), dihydrobromide (HOH)	250	200 100	0 +1	6/10 10/10
Tetramethylthiuram monosulfide (PG)	150	100 50	+2 >+15	10/10 3/10
β-Diisobutylaminoethylisothiourea dihydrochloride (HOH)	75	50 25	0 −2	10/10 10/10
2,2'-Pentamethylene-bis(1-acetyl-2-thiopseudourea), dihydrochloride (HOH)	250	200 100	−1 −3	10/10 10/10
2-Decyl-2-thiopseudourea, monohydrochloride (HOH)	75	25 10	0 +4	9/10 6/10
2-(Cyanomethyl)-2-thiopseudourea, monohydrochloride (HOH)	750	500 300	+7 0	5/10 8/10
2-(Amidinothio)butyric acid, monohydrobromide (HOH)	750	500 300	−10 −2	10/10 9/10
4-(Amidinothio)butyric acid, monohydrobromide (HOH)	100	50 25	−8 0	10/10 10/10
2-(2-Hydroxyethyl)-2-thiopseudourea, monohydrobromide (HOH)	400	300 200	−3 +1	10/10 7/10

Allylhydroxyethylthiourea (HOH)	>1000	1000 500	0 −1	9/10 10/10
2-(3-Hydroxypropyl)-2-thiopseudourea, monohydrobromide (HOH)	500	300 100 50	+2 −4 +2	4/5 10/10 10/10
2-(2-Methoxyethyl)-2-thiopseudourea, monohydrobromide (HOH)	400	300 200	−3 +7	7/10 7/10
1,1'-Dithioformamidine dihydrochloride (HOH)	200	100 50	−4 +3	10/10 10/10
2,2'-Ethylene-bis(2-thiopseudourea), dihydrobromide (HOH)	75	50 25	−2 −1	10/10 10/10
2,2'-(2-Butenylene)bis(2-thiopseudourea), dihydrochloride (HOH)	75	50 25	+1 +3	10/10 10/10
2,2'-(2-Butynylene)bis(2-thiopseudourea), dihydrochloride (HOH)	100	50 25	>+22 +3	2/8 10/10
2,2'-Pentamethylene-bis(2-thiopseudourea), dihydrobromide (HOH)	150	100 50	+1 +2	10/10 10/10
2,2'-Oxydiethylene-bis(2-thiopseudourea), dihydrochloride (HOH)	400	200 100	0 +3	10/10 10/10
1,1'-Ethylene-bis[3-2-(amidinethio)ethyl urea], dihydrochloride (PG)	100	50 25	+2 −2	10/10 10/10
1,3-Bis-2-(amidinothio)ethylurea, dihydrochloride (HOH)	225	100 50	−1 +2	6/10 10/10
2,2'-Tetramethylene-bis(2-thiopseudourea), dihydrobromide (HOH)	250	200 100 50	−5 +3 +3	10/10 10/10 10/10
Tetraethylthiuram disulfide (PG)	75	50 25	−1 >+15	10/10 5/10
Cyclopentylisothiourea hydrobromide (HOH)	250	200 100 50	+4 0 −3	4/4 10/10 10/10
1-Phenyl-2-thiourea (HOH)	40	10 5	−6 +1	10/10 10/10

1-o-Tolyl-2-thiourea (PG)	150	100 50	+3 −2	8/10 10/10
2-(2-Phenoxyethyl)-2-thiopseudourea, monohydrochloride (HOH)	40	25 10	−2 +1	10/10 10/10
p-Acetylaminoacetophenone thiosemicarbazone (PG)	50	25 10	−2 −1	10/10 7/10
2-(p-Nitrobenzyl)-2-thiopseudourea, monohydrochloride (HOH)	75	50 25	+1 −4	10/10 10/10
p-Nitrobenzylisothiourea hydrobromide (HOH)	150	100 50	−2 −4	9/10 10/10
p-Nitrophenylsulfonylurea (PG)	750	500 300	+2 −2	8/10 10/10
N-Sulfanilylurea (HOH)	>1000	1000 500	+1 −1	10/10 9/10
N-(p-Acetylaminobenzenesulfonyl)ethylurethane (PG)	750	500 300	−3 −2	10/10 10/10
p,p'-Biphenylene-bis-1,1'-(2-thiourea) (PG)	75	50 25	−6 −6	10/10 10/10
Di-p-methoxyphenylthiourea (PG)	750	500 300	−4 −4	10/10 10/10
Di-p-chlorophenylthiourea (PG)	150	100 50	0 −3	10/10 10/10
1-Isothiourea-2-dibenzylaminoethane dihydrochloride (HOH)	100	50 25	−6 −1	10/10 9/10
1-(p-Phenylazo)phenyl-2-thiourea (PG)	150	100 50	+1 −2	7/10 9/10
Bis-[p,p-(isothioureidomethyl)phenyl] sulfone dihydrochloride (HOH)	75	50 25	−5 −5	10/10 10/10

AMINES

Compound and vehicle used for toxicity and radiation tests	Toxicity	Radiation studies		
	Approx. LD_{50} (mg./kg.)	Dose (mg./kg.)	Change in ST_{50} (days)	Mortality at 30 days
Methylamine hydrochloride (HOH)	>1000	1000 500	−2 −2	10/10 10/10
N-(2-Nitro-2-methylbutyl)dimethylamine (PG)	200	100 50	+1 +3	10/10 10/10
N-(2-Nitroisobutyl)-N-methylglucamine (HOH)	>1000	1000 500	−2 0	10/10 10/10
Benzyloctylmethylamine (PG)	100	50 25	+3 −1	10/10 8/10
Ethylamine: 2-bromohydrobromide (HOH)	>1000	200 100	−2 +2	10/10 10/10
Ethylamine: 2-methoxy (65%-70% in HOH) (HOH)	400	200 100	−1 −4	10/10 10/10
2-Bromoethylamine hydrobromide (HOH)	400	200 100	−6 0	10/10 10/10
2,2'-Dithio-bis-(ethylamine) dihydrochloride (HOH)	750	300 200	>+16 0	0/10 7/10
Di(β-p-methoxyphenylethyl)amine hydrochloride (PG)	500	300 200	+3 −1	8/10 10/10
3-(N-Methylisopropylamino)-3-methyl-2-butanone hydrochloride (HOH)	150	100 50	−1 0	10/10 10/10
tert-Butyl-tert-amylamine hydrochloride (HOH)	100	50 25	−4 −2	10/10 10/10
3-tert-Butylamino-3-methyl-1-butene hydrochloride (HOH)	75	50 25	0 −5	10/10 10/10
3-tert-Butylamino-3-methyl-1-butyne hydrochloride (HOH)	75	50 25	−4 −2	10/10 10/10
3-Methyl-N-(2-o-propylphenoxyethyl) butylamine, monohydrochloride (HOH)	>1000	1000 500	−10 −3	9/10 10/10
3,5-Dimethyl-3-amino-1-hexyne hydrochloride (HOH)	400	100 50	−5 [illegible]	10/10 10/10

N-(2-Nitroisobutyl)-2-ethylhexylamine (PG)	250	200 100	−2 +3	10/10 10/10
p-Isopropylbenzylhexylamine sulfate (PG)	150	100 50	−10 +1	10/10 10 10
N-Heptyltaurine, monosodium salt (HOH)	>1000	1000 500	+9 +3	5 10 10 10
p-Isopropylbenzylheptylamine sulfate (PG)	75	50 25	−7 −4	10/10 10/10
Octylamine (PG)	100	50 25	−1 +6	10/10 9 10
Benzyloctylamine (PG)	100	50 25	−7 +1	10 10 9 10
p-Isopropylbenzyloctylamine (PG)	75	25 10	−8 +1	10/10 9 10
Dodecylamine (PG)	50	25 10	−3 +6	10/10 10 10
N-Dodecyltaurine, monosodium salt (HOH)	400	300 200	0 +2	10/10 10 10
Hexadecylamine (PG)	200	100 50	−1 +1	10/10 10/10
Octadecylamine (PG)	250	200 100	−3 0	10/10 10/10
N',N'-Dimethyl-1,2-butanediamine (PG)	150	100 50	−4 +1	10/10 10 10
N,N'-Bis(β-mercaptoethyl)hexamethylene diamine (PG)	350	200 100	−5 0	10/10 8/10
Armeen-CD-oleylamine (PG)	25	10 5	+2 +3	10/10 10 10
Armeen-TD-hydrogenated tallow amine (PG)	200	100 50	−1 +3	10/10 10 10
trans-1,2-Bis(aminoethyl)cyclobutane (HOH)	50	40 25	0 −3	9/10 10/10
1,3-Diamino-2,2,4,4-tetramethylcyclobutane (HOH)	450	200 100	−1 +1	10/10 10 10
Cyclobutane-1,2-bis(methylammonium) distearate (PG)	>1000	1000 750 500 500	−1 >+19 0 +2	8/10 3 10 5/10 9/10

Tetramethylammonium chloride (HOH)	25	7.5 5.0	+2 +2	9/10 10/10
Tetramethylammonium iodide (HOH)	40	10 5	0 +2	10/10 10/10
Aniline hydrochloride (HOH)	750	500 200	−4 −2	10/10 10/10
o-Toluidine (PG)	150	100 50	−1 −2	10/10 10/10
m-Toluidine (PG)	150	100 50	−1 −1	10/10 10/10
p-Toluidine (PG)	50	25 10	−2 +1	10/10 10/10
N-Acetyl-m-methylthioaniline (PG)	750	500 300	−2 −5	10/10 10/10
p-Nitroaniline (PG)	250	200 100	−3 +5	10/10 10/10
o-Phenylenediamine dihydrochloride (HOH)	250	200 100	−3 −1	10/10 10/10
m-Phenylenediamine dihydrochloride (HOH)	150	100 50	−4 0	9/10 10/10
2-Chlorobenzylethylenediamine (PG)	150	100 50	−2 −4	10/10 9/10
N,N-Dimethyl-p-phenylenediamine dihydrochloride (HOH)	40	25 10	+2 0	10/10 10/10
Diphenylbenzidine (sesame oil)	>1000	500 300	−2 +1	10/10 10/10
o,o-Dithio-bis-aniline (PG)	75	50 25	−6 −1	8/10 9/10
Benzyl-2,4-dichlorobenzylamine hydrochloride (PG)	250	200 100	−5 +2	10/10 6/10
Benzyl-3,4-dichlorobenzylamine hydrochloride (PG)	150	100 50	−3 −1	10/10 10/10
N-(2-Dimethylaminoethoxy)-N-(3,4,5-trimethoxybenzoyl)benzylamine hydrochloride (Tigan) (HOH)	400	300 100	+2 0	7/10 9/10
Dimethyl-α-naphthylamine (PG)	75	50 25	−3 0	10/10 10/10

N-(1-Naphthyi)ethylenediamine dihydrochloride (HOH)	150	100 50	+1 −2	10/10 10/10
2-Nitro-4-acetyl-2′-formylaminodiphenyl sulfide (PG)	250	200 100	−2 −7	10/10 10/10
N-(γ-Dimethylaminopropyl)-2-methyl thiodiphenylamine hydrochloride (HOH)	50	25 10	+2 −2	10/10 10/10
Hydroxylamine hydrochloride (HOH)	100	50 25	−4 −1	10/10 10/10
o-Benzylhydroxylamine hydrochloride (HOH)	250	200 100	−2 +1	10/10 9/10

GUANIDINES AND NITRILES

Compound and vehicle used for toxicity and radiation tests	Toxicity	Radiation studies		
	Approx LD_{50} (mg./kg.)	Dose (mg./kg.)	Change in ST_{50} (days)	Mortality at 30 days
Cyanoguanidine (HOH)	>1000	1000	0	10/10
		500	0	10/10
β-Phenethylbiguanide hydrochloride (HOH)	150	100	+2	4/4
		50	−1	10/10
		25	+1	10/10
Dipyridylguanidine trihydrochloride (HOH)	750	500	−2	10/10
		300	−7	10/10
Methyl cyanoacetate (HOH)	750	500	+5	10/10
		300	−2	10/10
Dimethylcyanamide (HOH)	40	25	−4	10/10
		10	−2	10/10
Propionitrile (HOH)	50	25	−4	9/10
		10	+1	10/10
Acrylonitrile (HOH)	75	75	+1	10/10
		50	+18	2/10
		25	−5	10/10
Cyanoacetamide (HOH)	750	500	0	10/10
		300	−4	10/10
Adiponitrile (HOH)	40	25	+1	10/10
		10	−4	10/10
Ethyl cyanoacetate (HOH)	750	500	+2	10/10
		300	−4	10/10
Methacrylonitrile (PG)	100	50	+3	5/10
		75	>+19	1/10
Hydroxyacrylonitrile (HOH)	>1000	1000	−2	10/10
		500	0	10/10
α,α'-Azodiisobutyronitrile (PG)	25	10	−2	10/10
		5	−3	10/10
trans-1,2-Dicyanocyclobutane (HOH)	275	250	−7	10/10
		100	−2	10/10
		50	+10	6/10
		50	0	10/10
		25	+1	10/10
1,2-Dicyanocyclobutene-1 (HOH)	150	100	0	9/10
		50	+1	10/10

3-Methylenecyclobutane carbonitrile (HOH)	250	200 100	0 0	10/10 10/10
Chlorinated-1,2-dicyanocyclobutane (Lot No. ST-15) (PG)	75	50 25	−4 −1	9/10 9/10
trans-2-Cyanocyclobutanecarboxamide (PG)	250	250 200 200 150 150 100 50	+3 +1 0 +15 +6 +3 +4	10/10 5/10 7/10 5/10 10/10 6/10 10/10
2,2-Dimethyl-3-methylenecyclobutane carbonitrile (HOH)	200	100 50	+2 0	10/10 10/10
Chlorinated-1,2-dicyanocyclobutane (Lot No. ST-24) (PG)	400	200 100 50	−4 −3 −4	10/10 10/10 10/10
Tetra-β-cyanoethyl-1,2-bis(aminomethyl) cyclobutane (HOH)	400	100 50	0 0	10/10 9/10
o-Chlorobenzonitrile (PG)	150	100 50	−4 +3	10/10 7/10
p-Chlorobenzonitrile (PG)	150	100 50	−2 0	10/10 10/10
Phenylacetonitrile (PG)	40	10 5	−6 −4	10/10 10/10
α-Dimethylaminophenylacetonitrile (PG)	40	25 10	+3 −1	8/10 9/10
4-Hydroxybenzonitrile (HOH)	200	100 50	−6 −5	10/10 10/10
m-Trifluoromethylphenylacetonitrile (PG)	100	50 25	+1 +3	8/10 7/10
3,4-Dihydro-2-cyano-2H-pyran (HOH)	250	200 100	−1 +2	10/10 10/10
Thiocyanic acid, α-3,α-5-bis(dimethylamino)-4-hydroxy-3,5-xylyl ester (PG)	75	50 25	+5 +2	7/10 9/10
Diphenylacetonitrile (PG)	200	100 50	−3 +2	10/10 10/10
4,4'-Biphenyldicarbonitrile (PG)	75	50 25	−5 −7	9/10 10/10

β-Cyanoethylmercaptan (HOH)	100	75 50	+1 +3	10/10 10/10
Sodium β-sulfopropionitrile (HOH)	>1000	500 300	−1 −2	10/10 10/10
p-Cetoxyphenylisothiocyanate (PG)	150	100 50	−5 +1	10/10 10/10
Cyclohexylcyanoethylethanolamine (PG)	200	100 25	−4 −1	10/10 10/10
p-(n)Dodecoxyphenylisot .iocyanate (PG)	150	50 25	−2 −1	10/10 10/10
2-Thio-m-thiazone-2,4-dione (HOH)	750	400 200	−1 −4	10/10 10/10

HYDRAZINES

Compound and vehicle used for toxicity and radiation tests	Toxicity	Radiation studies		
	Approx. LD_{50} (mg./kg.)	Dose (mg./kg.)	Change in ST_{50} (days)	Mortality at 30 days
Hydrazine sulfate (HOH)	250	100	−2	10/10
		50	−2	10/10
(3-Octylaminopropyl)hydrazine (PG)	15	10	+3	10/10
		5	+2	10/10
		1	−5	10/10
29 (2,2-Dimethylhydrazino)-3,6,9,12,15,18, 21,24,27-nonathianonacosane-1-thiol (PG)	400	400	−3	10/10
		300	>+17	4/10
		250	−4	10/10
		200	−6	10/10
		50	−4	8/10
Methylcyclopropanecarbonylhydrazine (HOH)	40	25	0	10/10
		10	−3	10/10
1,2-Cyclobutanedicarboxylic acid dihydrazide (HOH)	>1000	500	−1	10/10
		300	0	10/10
1,2-Cyclobutanedicarboxylic acid mono(2',2'-dimethyl)hydrazide (HOH)	>1000	1000	−1	10/10
		500	+4	10/10
Acetphenylhydrazine (PG)	150	100	−1	10/10
		50	−1	10/10
N-Benzyl-N'-isopropylhydrazine hydrochloride (HOH)	250	200	−2	10/10
		100	0	10/10
		20	−4	10/10
3,4,5-Trimethylacetophenonethiosemicarbazone (PG)	75	50	−10	10/10
		25	−8	10/10
3,3'-Thiodipropionic acid, bis(D-galactosylmethylenehydrazide) (PG)	750	500	0	10/10
		300	−1	10/10
1-Isonicotinyl-2-dimethylhydrazine (PG)	400	300	+1	10/10
		100	+1	10/10
		30	−2	9/10
1-Ethyl-2-isonicotinylhydrazine (HOH)	150	100	+1	10/10
		50	0	10/10
		10	−5	10/10
1-Isonicotinyl-2-ethylidenehydrazine (PG)	150	100	+1	10/10
		50	0	10/10
		10	−2	7/10

[α-(Methylmercapto)-4-pyridylmethylene] hydrazine (PG)	200	100 50 10	−2 −2 −4	10/10 10/10 6/10
α-(Benzylmercapto)-4-pyridylmethylene hydrazine (PG)	3	1.0 0.5 0.1	+1 +2 −5	10/10 10/10 10/10
1-Isonicotinyi-2-glucosylhydrazine (PG)	400	300 100 30	−2 0 −4	10/10 10/10 10/10
N,N'-Ethyleneidene-bis(isonicotinyl-hydrazine) (Safflower oil)	>1000	1000 500	0 -3	10/10 10/10

THIOPHENES, OXACYCLOPENTANES, AZACYCLOPENTANES, AND AZACYCLOHEXANES

Compound and vehicle used for toxicity and radiation tests	Toxicity	Radiation studies		
	Approx. LD_{50} (mg./kg.)	Dose (mg./kg.)	Change in ST_{50} (days)	Mortality at 30 days
2-Acetothiophene (PG)	40	10 200	−2 −1	10/10 10/10
4'-Hydroxy-5-nitro-2-furanacrylanilide (PG)	400	300 200	+1 −1	7/10 10/10
4'-(2-Chloroethylthio)-5-nitro-2-furan-acrylanilide (PG)	200	100 50	−3 −1	10/10 10/10
p-[3-(5-Nitro-2-furyl)acrylamido]benzyl-thioacetic acid, methyl ester (PG)	750	500 300	−3 −1	5/10 10/10
N-Butylenepyrrolidine (HOH)	50	25 10	−2 +3	10/10 9/10
Monothiosuccinimide (PG)	150	100 50	+3 +10	6/10 6/10
N-Methylmonothiosuccinimide (PG)	250	200 100	−2 +3	7/10 10/10
2-[2-(1-Pyrrolidinyl)ethyl]-2-thiopseudourea, dihydrochloride (HOH)	150	100 50	−2 −1	10/10 10/10
N-Phenylmonothiosuccinimide (PG)	250	200 100	+22 +1	4/10 10/10
N-(p-Methoxyphenyl)monothiosuccinimide (PG)	250	200 100	−1 +4	5/10 6/10
Pyrrolidinopropiophenone hydrochloride (HOH)	75	50 25	−3 −2	10/10 10/10
1-(1-Pyrrolidinocyclohexyl)methylthio-sulfuric acid, zwitterion (I) (HOH)	150	100 50	+2 0	5/6 10/10
1,2-Cyclobutanedicarboxamide (HOH)	>1000	1500 1000 1000 500	0 +4 −1 +1	10/10 5/10 10/10 6/10
1-Aza-2-imino-7-oxacycloheptane (HOH)	>1000	1500 1000 1000 500	+2 +5 −1 −2	10/10 6/10 10/10 10/10

1-Aza-2,7-diiminocycloheptane (HOH)	250	200 100	0 +2	10/10 10/10
N-(α-Naphthyl)-1,2-cyclobutanedicarboximide (PG)	750	500 300 100	−4 −3 +2	10/10 10/10 8/10
N-(β-Naphthyl)-1,2-cyclobutane dicarboximide (PG)	400	300 100	+2 +3	10/10 10/10
5-Acetyl-3-(2-aminoethyl)indole hydrochloride (HOH)	200	100 25	>+19 >+19	1/9 4/10
3-(2-Aminopropyl)-5-indolyl maleate salt (HOH)	625	500 300	+4 −1	3/8 6/10
DL-3-(2-Amino-1-methylethyl)-5-propionylindole hydrochloride (HOH)	200	100 50	+1 +2	13/17 8/10
DL-3-(Aminopropylene)indolyl-5-phenylketone hydrochloride (HOH)	100	50 25	+3 −2	8/10 9/9
3-Amino-9-ethylcarbazole (PG)	150	100 50	−10 +1	10/10 5/10
3,6-Diamino-9-ethylcarbazole (PG)	150	100 50	−2 0	10/10 9/10
3-Methyl-5-carboxytetrahydro-4-carboline (PG)	150	100 50	0 +1	10/10 10/10
Ajmaline (PG)	75	50 25	+2 +1	9/10 10/10
Aspidospermine (PG)	40	25 10	−1 −2	10/10 8/10
Spiroxyine hydrochloride hemihydrate (HOH)	500	300 100	−3 −2	7/7 10/10
18-Benzylidene-17-hydroxy-yohimbane (PG)	250	200 100	>+19 −2	1/10 9/10
Monothioglutarimide (PG)	100	50 25	>+17 +3	3/9 10/10
2-Iminopiperidine hydrochloride (HOH)	150	50 25	+1 −5	8/10 10/10
N-(2-Nitroisobutyl)piperidine (PG)	200	100 50	−1 +3	10/10 10/10

1-Piperidine ethanethiol, monohydrochloride (HOH)	75	50 25	0 −1	10/10 10/10
1-Methyl-p-aminoethylthioazocyclohexane (HOH)	250	200 100	−4 0	10/10 10/10
1-[(2-Mercaptoethylthio)methyl]-4-methyl piperazine, polymer (PG)	200	100 50	−5 −1	9/10 10/10
4-Piperidinobenzaldehyde thiosemicarbazone (PG)	75	25 10	+1 −5	4/10 10/10
1-Phenyl-1-cyclopentyl-3-piperidino-1-propanol hydrochloride (HOH)	250	100 50	−3 −2	10/10 10/10
Isocinchomeronic acid (pyridine 2,5-dicarboxylic acid) (HOH + $NaHCO_3$)	>1000	1000 500	−6 0	10/10 10/10
2-Mercaptopyridine (PG)	250	200 100	−5 −5	10/10 10/10
Zinc derivative of 3-pyridinethiol (PG)	150	100 50	−2 +4	10/10 8/10
Pyridoxal hydrochloride (HOH)	400	300 200	−1 −2	9/10 9/10
Thioisonicotinamide (PG)	250	200 100	+1 −1	10/10 10/10
Thioisonicotinamide-1-oxide (HOH)	750	500 300	0 0	10/10 10/10
Isonicotinaldehyde thiosemicarbazone (PG)	150	100 50	−2 −1	10/10 10/10
Nicotinaldehyde thiosemicarbazone hydrochloride (HOH)	150	100 50	−3 −3	10/10 10/10
Methyl-2-pyridyl ketone thiosemicarbazone (PG)	5	2 1	+2 −1	10/10 10/10
Methyl-3-pyridyl ketone thiosemicarbazone (PG)	25	10 5	−1 0	10/10 10/10
Nicotinylthiosemicarbazide hydrochloride (HOH)	750	500 300	+1 0	10/10 10/10
Trimethylamine isonicotinamide (PG)	450	300 200	+2 +5	10/10 10/10

Isonicotinamidoguanylmercaptoacetic acid hydrochloride (HOH)	750	500 300	+1 0	10/10 10/10
Benzyl-4-benzylpyridinium chloride (HOH)	75	50 25	−3 0	10/10 10/10
Quinoline (synthetic) (PG)	200	100 50	+3 +9	7/11 6 10
Isoquinoline (PG)	150	100 50	−4 −1	10/10 10/10
6-Quinolinecarboxylic acid (HOH + $NaHCO_3$)	>1000	1000 500	−2 +2	10/10 8 9
3-Hydroxycinchoninic acid (PG)	250	200 100	−1 0	9/10 10 10
3-Hydrazinoquinoline dihydrochloride (HOH)	250	200 100	>+18 >+22	5 10 3 9
6-Methoxy-8-aminoquinoline (PG)	25	10 5	+2 −4	10 10 10/10
2-Hydroxy-3-n-butyl-9,10-dimethoxy-1, 2,3,4,5,7-hexahydro-benzo(a)quinolizine hydrochloride (HOH)	150	100 50	−3 −1	10 10 10/10
6-Heptyl-4-quinolinol-1-oxide (PG)	450	300 200	−3 +1	10 10 10 10
2-Methyl-1,4-naphthoquinone-1-thiosemicarbazone (PG)	75	50 25	−2 −2	10/10 10/10
7-Chloro-4-[(2-diethyl)aminoethylamino] quinoline-1-oxide (PG)	150	100 50	+1 0	10/10 9/10
7-Chloro-4-[3-(1-pyrrolidinyl)propylamino] quinoline,1-oxide (PG)	150	100 50	0 +2	10 10 10 10
Cinchophen (PG)	200	100 50	−3 −5	10/10 10/10
1,7-Bis(N-tetrahydroisoquinolyl)heptane dihydrochloride (HOH)	250	50 25	−2 −3	10 10 9/10
1,10-Bis(N-tetrahydroisoquinolyl)decane dihydrochloride (PG)	150	50 25	+1 −2	10 10 10 10

2,3,3a,5,6,11,12,12a-Octahydro-8 hydroxy-1H-isoquino(2,1a)(1)pyridinium bromide (HOH)	75	25 10	−2 −1	10/10 7/7
7-[2-Hydroxy-3-(N-2-hydroxyethyl-N-methylamino)-propyl]-1,3-dimethylxanthinepyridine-3-carboxylate (Complamex) (HOH)	>1000	1000 500 250 50	0 +3 −2 −4	10/10 10/10 10/10 10/10

OXAZOLES AND OXAZINES

Compound and vehicle used for toxicity and radiation tests	Toxicity	Radiation studies		
	Approx. LD_{50} (mg./kg.)	Dose (mg./kg.)	Change in ST_{50} (days)	Mortality at 30 days
3-(2-Hydroxyethyl)-2-oxazolidinone (HOH)	750	500 300	−1 −1	10/10 10/10
2-[2-(4-Morpholinyl)ether]-2-thiopseudourea, dihydrochloride (HOH)	40	25 10	0 −3	10/10 10/10
N-[2-Amidinothio)ethyl]-4-morpholine-carboxamide, monohydrochloride (HOH)	750	500 300	+4 +2	6/10 10/10
4-{ [(2-Diethylaminoethyl)thio]methyl }-4-methylmorpholinium-p-toluenesulfonate metho-p-toluenesulfonate (HOH)	100	50 25	−2 0	10/10 9/10
4-[2-(Diethylaminomethylthio)ethyl]-4-methylmorpholinium-p-toluenesulfonate metho-p-toluenesulfonate (HOH)	50	25 10	−4 0	10/10 10/10
2-Imino-4-methyl-5-phenyloxazoline (PG)	10	5 1	+3 −4	10/10 9/10
4-Morpholinobenzaldehyde thiosemicarbazone (PG)	75	50 25	+5 −5	9/10 10/10
n-Heptyl ester of 4-(γ-morpholine propoxy) benzoic acid hydrochloride (HOH)	500	300 200	−7 −3	10/10 10/10

THIAZOLES AND THIAZINES

Compound and vehicle used for toxicity and radiation tests	Toxicity	Radiation studies		
	Approx. LD_{50} (mg./kg.)	Dose (mg./kg.)	Change in ST_{50} (days)	Mortality at 30 days
2-Amino-2-thiazoline (PG)	150	100 50	−1 −5	10/10 10/10
2,4-Thiazolidinedione (PG)	750	300 200	−1 +2	10/10 10/10
2,4-Dimethylthiazole (PG)	250	200 100	0 0	9/10 10/10
Thiazolidine-4-carboxylic acid (HOH)	150	100 50	+7 0	10/10 7/10
Penicillamine (HOH)	350	300 100	+1 +1	8/10 10/10
6-Aminopenicillanic acid (PG)	>1000	500 300	+1 −1	10/10 10/10
5-(p-Chlorobenzylidene)-2-thiothiazolidine-2,4-dione (PG)	75	50 25	+6 −8	9/10 10/10
2-Thioureido-4-(p-nitrophenyl)thiazole (PG)	150	100 50	0 −8	7/10 10/10
5-(p-Dimethylaminobenzoylidene)rhodanine (PG)	150	100 50	+2 −3	9/10 9/10
5-Benzylidene-2-phenylimino-4-thiazolidinone (PG)	75	50 25	+1 −2	8/10 10/10
5-(p-Acetamidobenzylidene)-3-(p-acetamidobenzoylideneamino)rhodanine (PG)	100	50 25	+1 −4	6/10 8/10
6-Ethoxy-2-mercaptobenzothiazole (PG)	250	200 100	−2 +2	10/10 8/10
5-Chloro-2-mercaptobenzothiazole (PG)	150	100 50	+2 −5	10/10 10/10
2-(Dimethylaminomethylthio)benzothiazole (HOH)	150	100 50	+1 −6	10/10 10/10
Ethyl-3-methyl-4-oxo-5-piperidino-2,4-thiazolidine acetate (PG)	400	400 200	−1 0	9/10 9/10
2-Amino-4,5-diphenylthiazole (PG)	200	200 100	−7 −4	10/10 10/10

2,5-Bis(4-pyridyl)-1,3,4-thiadiazole (PG)	100	100 50	−4 0	10 10 10 10
5-Benzylidenerhodanine (PG)	75	50 25	−2 −2	10 10 10 10
3-Amino-5-benzylidenerhodanine (PG)	100	50 25	+1 +2	10/10 10/10
5-Benzylidene-3-benzylideneaminorhodanine (PG)	250	200 100	+1 0	8 10 9/10
5-Benzylidene-3-salicylideneaminorhodanine (PG)	75	50 40 25 15	−1 −3 >+22 0	10/10 10/10 4/10 10/10
2-(p-Methoxybenzylidenehydrazino)-4-oxo-5-thiazolidineacetic acid (HOH + $NaHCO_3$)	>1000	500 300	+3 +2	10/10 10/10
2-[(p-Acetamidobenzylidene)hydrazino]-4-oxo-5-thiazolidineacetic acid (HOH + $NaHCO_3$)	100	50 25	−1 +2	10/10 10/10
5,5'-Methylidynedirhodanine with triethylamine (PG)	150	100 50	−3 −5	10/10 10/10
2,2-Dimethyl-3-thiomorpholone (PG)	400	250 100	−3 +2	10 10 8/10
2,2-Diethyl-3-thiamorpholone (PG)	250	200 100	−1 −2	8/10 10 10
2-Methyl-1,5-benzothiazepin-4-(5H)-one (PG)	400	300 200	+2 +3	10/10 10/10
4-Methyl-1,5-benzothiazepin-2-(3H)-one (PG)	400	300 200	−1 +1	6/9 10/10
2,3-Dihydro-1,5-benzothiazepin-4-(5H)-one (PG)	750	500 300	0 +3	9/10 10/10
2,3-Dihydro-7-methyl-1,5-benzothiazepin-4-(5H)-one,1,1-dioxide (PG)	400	300 200	+7 +2	7/10 10/10
2,3,4,5-Tetrahydro-1,5-benzothiazepin, monohydrochioride (HOH)	400	300 200	+19 +3	4 8 10 10
Thionine (HOH)	400	300 200	−3 −3	10/10 10/10
Methylene blue chloride (HOH)	150	100 50	−5 −2	10/10 10/10
(2-Chlorophenothiazino)propylbiguanide hydrochloride (HOH)	100	50 25	−4 −8	10/10 10/10

DIAZOLES AND DIAZINES

Compound and vehicle used for toxicity and radiation tests	Toxicity	Radiation studies		
	Approx. LD_{50} (mg./kg.)	Dose (mg./kg.)	Change in ST_{50} (days)	Mortality at 30 days
1-Isopropyl-2-(2-furyl)-4,4-dimethyl-imidazolidine (PG)	250	200 100	−3 0	10/10 10/10
1,2-Diphenyl-4,4-dimethylimidazolidine (PG)	150	100 50	−1 +1	10/10 10/10
1-(1,1-Dimethyl-2-hydroxyethyl)-4,4-dimethyl-2-imidazolidinethione (PG)	250	200 100	0 0	10/10 10/10
1-Isopropyl-4,4-dimethyl-2-imidazolidine-thione (PG)	150	100 50	0 +5	8/10 10/10
1-Butyl-4,4-dimethyl-2-imidazolidinethione (PG)	150	100 50	−5 +1	10/10 10/10
1-(1,1,3,3-Tetramethylbutyl)-4,4-dimethyl-2-imidazolidinethione (PG)	100	50 25	−5 +1	10/10 10/10
1-Octadecyl-4,4-dimethyl-2-imidazolidine-thione (PG)	250	200 100	−1 −2	10/10 10/10
1-Phenyl-4,4-dimethyl-2-imidazolidinethione (PG)	200	100 50	0 +1	10/10 10/10
2-[(p-Nitrobenzyl)thio]-2-imidazoline, monohydrobromide (HOH)	50	25 10	−1 +1	10/10 10/10
2-[(m-Chlorobenzyl)thio]-2-imidazoline, monohydrobromide (HOH)	75	25 10	+1 +1	10/10 10/10
2,2-{[(Tetrachloro-p-phenylene)methylene] thio}-di-2-imidazoline, dihydrochloride (HOH)	150	100 50	−1 0	6/7 10/10
2-[2-(Diethylamino)ethyl]-5-methyl-2H-(1)benzothiopyrano-4,3,2-imidazole (PG)	200	100 50	−5 −2	10/10 10/10
6,7-Dihydro-3-methyl-1-5H-imidazo(2,1-β)thiazolium chloride (HOH)	75	50 25	−2 −1	10/10 10/10

2-Amino-1,3,4-thiadiazole, monohydrochloride (HOH)	250	200 100	−3 +2	10 10 10/10
5-Amino-1,3,4-thiadiazole-2-thiol (HOH)	350	200 100	+1 −2	8/10 10/10
2-Amino-5-mercapto-1,3,4-thiadiazole (PG)	250	200 100	+2 −2	5/10 10/10
2,5-Dimercapto-1,3,4-thiadiazole (HOH)	750	200 100	−5 −3	10 10 10/10
1,3,4-Thiadiazole-2,5-dithiol (PG)	150	100 50	−2 +3	10/10 10/10
2,2'-Dithio-bis(5-amino-1,3,4-thiadiazole) (PG)	150	100 50	−2 −3	10/10 9/10
2-Amino-5-(p-aminophenylmercapto)-1,3,4-thiadiazole (PG)	250	200 100	−1 −3	8/10 10/10
5-Anilino-1,3,4-thiadiazole-2-thiol (PG)	250	200 100	−1 0	8/10 10 10
2-(4-Pyridyl)-5-phenyl-1,3,4-thiadiazole (PG)	150	100 50	−2 0	10/10 10 10
2-Methyl-1,3,4-thiadiazole-5-phenylhydrazine (PG)	75	50 25	−2 −2	10/10 10 10
2-Phenyl-1,3,4-thiadiazole-5-sulfonamide (PG)	250	200 100	−1 0	10 10 9/10
3-Allyl-2-thiohydantoin (HOH)	250	200 100	0 +1	10/10 10/10
3-(2-Aminoethyl)-2-thiohydantoin (HOH)	400	300 200	−1 −3	10/10 10 10
3-Phenyl-2-thiohydantoin (PG)	75	25 10	+1 −5	9/10 10/10
3-Methyl-5-phenyl-5-(2-thienyl)hydantoin (PG)	150	100 50	−2 +3	10/10 10/10
5-Cyclohexylethyl-5-(2-thienyl)hydantoin (PG)	150	100 50	−5 0	10/10 8/10
3-Phenyl-5-(p-hydroxybenzyl)-2-thiohydantoin (PG)	150	100 50	−6 −7	10 10 10/10
5-Cyclohexylbutyl-5-(2-thienyl)hydantoin (PG)	200	100 50	−5 −4	10/10 10/10

1-Isonicotinyl-3,5-dimethylpyrazole (PG)	250	200 100	−2 −1	10/10 10/10
3,5-Dioxo-1,2-diphenyl-4-n-butylpyrazolidene (Butazolidin) (PG)	150	100 50	−5 0	9/10 9/10
3,5-Dioxo-1-phenyl-2-p-hydroxy-phenyl-4-n-butylpyrazolidene (Oxyphenbutazone) (PG)	150	100 50	−2 0	10/10 9/10
N-[(2,3-Dimethyl-5-oxo-1-phenyl)-3-pyrazolin-4-yl]-anthranilic acid (HOH + $NaHCO_3$)	100	50 25	+3 +2	8/10 10/10
1,2-Diphenyl-4-methylthioethyl-3,5-pyrazolidinedione (PG)	200	100 50	−1 >+15	10/10 9/10
1,2-Diphenyl-4-(2'-phenylsulfinethyl)-3,5-pyrazolidinedione (Sulfinpyrazone) (PG)	150	100 50	0 −2	8/10 9/10
Quinoxaline (PG)	250	200 100	>+18 >+22	3/10 1/10
2,3 Quinoxalinediol (PG)	200	100 50	−7 −2	7/10 7/10
2,3-Quinoxalinedithiol (PG)	100	50 25	−5 +3	10/10 9/10
2,3-Di-(p,p'-dimethoxystyryl)quinoxaline (PG)	250	100 50	−4 −3	10/10 10/10
4-Quinazolinol, 3-oxide (PG)	250	200 100	+2 −1	10/10 10/10
4-Quinazolinethiol (PG)	750	500 300	>+17 >+19	4/10 4/10
6-Chloro-4-quinazolinethiol (PG)	>1000	1000 500	−2 +2	10/10 10/10
3-Propyl-4-(3H)-quinazolinethione (PG)	200	100 50	0 −1	10/10 10/10
3,4-Dihydro-4-phenyl-2(1H)-quinazolinethione (PG)	75	50 25	0 +3	10/10 10/10
3-Benzyl-2,3-dihydro-2,2-dimethyl-4(1H)-quinazolinethione (PG)	450	300 200	−2 +4	10/10 10/10

3-(p-Acetylphenyl)-6-chloro-2-thio-2,4-(1H,3H)-quinazolinedione (PG)	250	200 100	−3 +2	10/10 10/10
7-Chloro-4-[(3-diethylaminopropyl)amino] quinoline-1-oxide (PG)	150	100 50	+1 +3	9/10 10/10
2-Dimethylaminopyrazine hydrochloride (HOH)	200	100 50	−3 −2	10/10 9/9
6-Amino-3-pyridazinethiol (PG)	400	300 100	+1 +2	10/10 8/10
Dithiothymine (PG)	200	100 50	0 +1	9/10 10/10
6-Aminouracil (sodium salt) (HOH)	>1000	500 300	−2 +1	10/10 10/10
2-Ethylthio-4-amino-6-oxypyrimidine (PG)	200	100 50	+2 0	6/10 7/10
5-Bromuracil (HOH + $NaHCO_3$)	>1000	1000 500	−6 −2	10/10 10/10
5-Carbethoxy-2-thiouracil (PG)	250	200 100	0 +1	10/10 5/10
4'-(1,4-Dihydro-2-mercapto-4,4,6-trimethyl-1-pyrimidinyl)acetophenone (PG)	75	50 25	−2 0	7/10 10/10
1,4-Dihydro-1-(o-mercaptophenyl)-4,4,6-trimethyl-2-pyrimidinethiol (PG)	400	250 100	−3 +2	10/10 8/10
1-Methylpiperazine (PG)	150	100 50	+1 −2	10/10 10/10
1-m-Methylbenzylpiperazine (PG)	100	50 25	+1 −1	10/10 10/10
N-Benzyl N'-benzoylpiperazine (HOH)	400	100 50	−5 −1	10/10 10/10
1-(3,4-Dichlorophenyl)-4-methoxypropyl piperazine sulfate (HOH)	250	200 100	−7 −2	10/10 10/10
1,4-Piperazinediacetic acid, dihydrate (PG)	>1000	500 300	−4 −3	10/10 10/10
2-Pyridylethylpiperazine (PG)	150	100 25	−6 0	10/10 10/10

α-Ethyl-3-methyl-6-oxo-1(6H)-pyridazine acetic acid hydrazide (PG)	625	500 300	>+19 +3	4/10 5/10
1-[(Ethylthio)methyl]-1,4-dimethylpiperazinium di-p-toluenesulfonate, polymer (HOH)	7.5	5 1	0 −1	10/10 10/10
Thiocyanic acid, 4-hydroxy-α-3-(4-methyl-1-piperazinyl)-3,5-xylyl ester (PG)	75	50 25	+1 +1	10/10 10/10
1-(2-Methoxyphenyl)-4-thiofuran (PG)	400	300 100	−4 −2	10/10 10/10
1,4-Dimethyl-1,4-bis[2-(morpholinomethyl-thio)ethyl]-piperazinium di-p-toluene-sulfonate bis(metho-p-toluene) sulfonate (HOH)	40	25 10	+1 +3	10/10 10/10
1,1,4-Trimethyl-4 { [2-(4-methyl-1-piperazinyl) ethylthio]methyl } piperazinium di-p-toluenesulfonate bis-(metho-p-toluene) sulfonate (HOH)	250	100 50	0 −3	9/10 10/10
6-Chloro-o-methyl-2H-1,2,4-benzothiadiazin-7-sulfohydroxamic acid, 1,1-dioxide hemihydrate (PG)	400	300 100	−5 −7	10/10 10/10
7-Chloro-2-(cyclopropylamino)-5-phenyl-3H-1,4-benzodiazepine-4-oxide (PG)	150	100 50	−1 −1	12/15 7/10

TRIAZOLES AND DIOXANES

Compound and vehicle used for toxicity and radiation tests	Toxicity	Radiation studies		
	Approx. LD_{50} (mg./kg.)	Dose (mg./kg.)	Change in ST_{50} (days)	Mortality at 30 days
S-Trithiane (Corn oil)	250	200 100	−2 −5	10/10 10/10
5-Amino-1H-1,2,4-triazole-3-carboxylic acid, sodium salt (HOH)	>1000	1000 500	0 −1	10/10 10/10
3-Mercapto-S-hydroxy-1,2,4-triazino-6-carboxylic acid (PG)	250	200 100	−3 −1	10/10 10/10
2,6-Diaminopurine sulfate (HOH + $NaHCO_3$)	250	200 100	−1 0	10/10 10/10
2-Thio-6-oxypurine (HOH + $NaHCO_3$)	625	500 300	−4 0	10/10 10/10
2,8-Dithio-6-oxypurine (HOH + $NaHCO_3$)	400	300 100	-4 0	10/10 10/10
p-(2-Amino-6-hydroxy-8-purinylazo)-benzenesulfonic acid (HOH)	>1000	1000 500	+2 −6	10/10 10/10
2,6-Bis-(diethylolamine)-4,8-dipiperidino-pyrimido-(5,4-d) (PG)	150	100 50	−1 −1	10/10 10/10
1-Phenyl-5-mercaptotetrazole (PG)	250	200 50	−11 −1	10/10 10/10
Hypoxanthine (HOH + $NaHCO_3$)	750	500 300	−1 −2	10/10 10/10
8-Azaguanine (HOH + $NaHCO_3$)	>1000	1000 500	−8 −2	10/10 10/10
1-Methyl-2-mercapto-4,7-dihydroxy-1,3,5,6-tetrazaindene (PG)	750	500 300	0 −7	8/10 10/10
1-Phenyl-2-mercapto-4,7-dihydroxy-1,3,5,6-tetrazaindene (PG)	250	200 100	+1 −2	8/10 9/10
7-Theophylline acetamide (1,2,3,6-Tetrahydro-1,3-dimethyl-2,6-dioxopurine-7-acetamide) (PG)	750	500 300	−1 −2	9/10 10/10

Ethyl-7-theophylline acetate (Ethyl-1,2,3,6-tetrahydro-1,3-dimethyl-2,6-dioxopurine-7-acetate) (PG)	>1000	1000 500	+2 +1	7/10 7/10
8-(2-Dimethylaminoethoxy)theophylline (1,3-Dimethyl-8-(2-dimethylamino-ethoxy) xanthine) (PG)	750	500 300	−3 >+19	9/10 4/10
7,7'-Trimethylene-bis { 8-[bis(2-hydroxy-ethyl)amino]theophylline } (PG)	1000	1000 500	>+19 −3	3/10 9/10
1,2-Cyclobutanedicarboguanamine (PG)	75	50 25	0 −2	10/10 10/10
1,2-Cyclobutanedicarboguanamine phosphate (HOH)	400	300 100	0 −1	10/10 10/10
1-Methyl-5-mercapto-1,2,3,4-tetrazole (PG)	400	300 200	−5 −11	10/10 10/10
2-Phenyl-1,5-benzothiazepin-4(5H)-one (PG)	400	300 200	−2 +7	7/10 5/10
2-(Benzylmethylamino)-7-chloro-5-phenyl-3H-1,4-benzodiazepine-4-oxide (PG)	300	200 100	+3 −2	7/10 10/10
5-Methyl-7-phenyl-3H-1,2-dithiepin-3-thione (PG)	250	200 100	+3 +1	7/10 8/9
7-Chloro-1-methyl-5-phenyl-1H-1,4-benzodiazepine-2(3H)-thione (PG)	250	200 50	0 −1	6/10 10/10
5-Nitro-5-methyl-1,3-dioxane (PG)	150	100 50	+2 +3	10/10 10/10
2-Methyl-3-ethanol benzodioxane (HOH)	400	300 100	−3 +1	10/10 10/10

MISCELLANEOUS

Compound and vehicle used for toxicity and radiation tests	Toxicity	Radiation studies		
	Approx. LD_{50} (mg./kg.)	Dose (mg./kg.)	Change in ST_{50} (days)	Mortality at 30 days
Calcium chloride (HOH)	>200	200 100	+1 −2	10/10 10/10
Sodium chlorate (HOH)	>1000	1000 500	−1 +1	10/10 10/10
Sodium borate, tetra (HOH)	>1000	1000 500	−1 +1	10/10 10/10
Sodium nitrite (HOH)		125 100	+6 0	9/10 8/10
2-Nitropropane (PG)	75	50 25	−3 +2	10/10 10/10
2,3-Dibromopropane (PG)	75	50 25	−4 −3	10/10 10/10
2-Bromopentane (PG)	150	100 50	−7 −3	10/10 10/10
1,3-Dibromopropane (HOH)	750	500 200	−1 0	10/10 10/10
Naphthalene (PG)	150	100 50	−2 −4	10/10 10/10
α-(Methoxymethyl)naphthalene (PG)	200	100 50	−6 −3	9/10 10/10
Calcium flavonate (HOH)	625	500 300	−4 +3	10/10 10/10
Vitamin B_{12} with intrinsic factor concentrate (HOH)	>1000	1000 500	−4 0	10/10 10/10
Corn oil	>50000	50000	0	10/10
Olive oil	>50000	50000	−1	10/10
Petrolatum (liquid)	>50000	50000	0	10/10
Safflower oil	>50000	1 cc.	+2	10/10
Sesame oil	>50000	50000	−1	9/10

INDEX

Unclassified
Security Classification

DOCUMENT CONTROL DATA - R & D

(Security classification of title, body of abstract and indexing annotation must be entered when the overall report is classified)

1 ORIGINATING ACTIVITY (Corporate author) USAF Radiation Laboratory University of Chicago Chicago, Ill.	2a. REPORT SECURITY CLASSIFICATION Unclassified 2b. GROUP

3 REPORT TITLE

A FURTHER SURVEY OF COMPOUNDS FOR RADIATION PROTECTION

4 DESCRIPTIVE NOTES (Type of report and inclusive dates)

Final report Jan. 1961 - Apr. 1965

5 AUTHOR(S) (First name, middle initial, last name)

Vivian Plzak
John Doull

6 REPORT DATE February 1969	7a. TOTAL NO. OF PAGES 82	7b. NO. OF REFS —
8a CONTRACT OR GRANT NO 41(609)-2977 b. PROJECT NO c. Task No. 775703 d.	9a. ORIGINATOR'S REPORT NUMBER(S) SAM-TR-69-1 9b. OTHER REPORT NO(S) (Any other numbers that may be assigned this report)	

10 DISTRIBUTION STATEMENT

This document has been approved for public release and sale; its distribution is unlimited.

11. SUPPLEMENTARY NOTES	12. SPONSORING MILITARY ACTIVITY USAF School of Aerospace Medicine Aerospace Medical Division (AFSC) Brooks Air Force Base, Texas

13. ABSTRACT

This report summarizes the results obtained with 617 compounds tested for their radioprotective activity in adult male mice irradiated with a control-demonstrated LD_{99+} of 800 R (250 kvp) x-rays. A compound was considered to exhibit radioprotective activity if it (1) permitted any of the treated mice to survive for 30 days after the otherwise lethal whole-body x-irradiation or (2) increased the median survival time of treated animals by 5 days or more beyond the median survival time of the untreated control mice (9 ± 3 days).

Of the 617 compounds tested, 245 successfully passed one or both of the stated specifications. Additionally, data are offered to allow comparisons of chemically related groups for structure-activity relationships, and to indicate the types of structures which offer the greatest promise as a source of more effective and less toxic radioprotective agents.

DD FORM 1 NOV 65 1473

Unclassified
Security Classification

14. KEY WORDS	LINK A		LINK B		LINK C	
	ROLE	WT	ROLE	WT	ROLE	WT
Radiobiology						
Radioprotective agents						
Toxicity of radioprotective agents						
Radioprotective activity						
Structure-activity relationships						